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900

=> S (WEYFIAAEE|EYFIAAEEV)/SQSP AND 3-10/SQL 2 WEYFIAAEE|EYFIAAEEV/SQSP 583950 3-10/SQL

L1 2 (WEYFIAAEE|EYFIAAEEV)/SQSP AND 3-10/SQL

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L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 499777-67-2 REGISTRY

ED Entered STN: 18 Mar 2003

CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4: PN: US20030040600 SEQID: 6 claimed sequence

CN 6: PN: US20030040600 SEQID: 6 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C61 H81 N11 O18

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 477192-10-2 REGISTRY

ED Entered STN: 19 Dec 2002

CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L-alanyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C50 H71 N9 O17

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

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 L3
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      ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 L3
 AN
      2005:346796 CAPLUS
 DN
      142:406541
 TI
      Hirudin-like peptides from C-terminus of human blood clotting factor Va
      heavy chain as prothrombinase inhibitors for use in treatment of blood
      clotting disorders
                             Applicant
      Kalafatis, Michael
 IN
      Cleveland State University, USA
 PA
 SO
      PCT Int. Appl., 88 pp.
      CODEN: PIXXD2
 DT
      Patent
 LΑ
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              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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              SN, TD, TG
                           Ρ
                                  20030912
 PRAI US 2003-502186P
      Disclosed are peptides from the carboxy terminus of the human blood
      clotting factor Va which significantly inhibit thrombin generation. Also
      disclosed are pharmaceutical compns. containing these peptides and related
      therapeutic methods for inhibiting thrombin generation and treating blood
      coagulation disorders. Thus, peptides DYDY and DYDYQ, and sulfonated
      derivs. thereof, compete with prothrombinase for binding to prothrombin.
 L3
      ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN SIN
 ΑN
      2003:155110 CAPLUS
 DN
      138:198622
 TΙ
      Peptides derived from amino acids 307 to 356 of the human blood
      coagulation factor Va as thrombin generation inhibitors
      Kalafatis, Michael; Mann, Kenneth Applicant
 IN
 PA
      Cleveland State University, USA
 SO
      U.S. Pat. Appl. Publ., 20 pp.
      CODEN: USXXCO
 DT
      Patent
 LΑ
      English
 FAN.CNT 1
      PATENT NO.
                          KIND
                                  DATE
                                              APPLICATION NO.
                                                                      DATE
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20030227 US 2001-911129

20010723

PΙ

US 2003040600

A1

US 6703364 B2 20040309 US 2004186271 A1 20040923 US 2004-795795 20040308 20010723

Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

ANSWER 3 OF 3, CAPLUS COPYRIGHT 2005 ACS on STN 9KK L3

Α3

2002:732142 CAPLUS ΑN

PRAI US 2001-911129

- 138:2631 DN
- TΙ Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X
- ΑU Kalafatis, Michael; Beck, Daniel O.
- CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115,
- Biochemistry (2002), 41(42), 12715-12728 ACLE EFD SO CODEN: BICHAW; ISSN: 0006-2960
- American Chemical Society PB
- DΤ Journal
- LΑ English
- The authors have recently shown that amino acid region 307-348 of factor AB Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 μM . the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 µM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

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=> S (WEYEIAAE|EYFIAAEE|YFIAAEEV)/SQSP AND 3-10/SQL 2 WEYEIAAE|EYFIAAEE|YFIAAEEV/SQSP 583950 3-10/SQL

L4 2 (WEYEIAAE|EYFIAAEE|YFIAAEEV)/SQSP AND 3-10/SQL

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- L4 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 499777-67-2 REGISTRY
- ED Entered STN: 18 Mar 2003
- CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

- CN 4: PN: US20030040600 SEQID: 6 claimed sequence
- CN 6: PN: US20030040600 SEQID: 6 claimed protein
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C61 H81 N11 O18
- SR CA
- LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

PAGE 1-A

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 477192-10-2 REGISTRY

ED Entered STN: 19 Dec 2002

CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C50 H71 N9 O17

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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SO

DT

LΑ

CODEN: USXXCO

Patent English

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FAN	CNT	1
r AN	. C.N.I.	- 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				
PI US 2003040600	A1	20030227	US 2001-911129	20010723
US 6703364	B2	20040309		
US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI US 2001-911129	A3	20010723		

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

- L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN V
- AN 2002:732142 CAPLUS
- DN 138:2631
- TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X
- AU Kalafatis, Michael; Beck, Daniel O.
- CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA
- SO Biochemistry (2002), 41(42), 12715-12728 after EFD CODEN: BICHAW; ISSN: 0006-2960
- PB American Chemical Society
- DT Journal
- LA English
- AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of $5.7 \mu M$. the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 μM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

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- L7 2 (WEYFIAA|EYFIAAE|YFIAAEE|FIAAEEV)/SQSP AND 3-10/SQL

=> D 1-2

- L7 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 499777-67-2 REGISTRY
- ED Entered STN: 18 Mar 2003
- CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4: PN: US20030040600 SEQID: 6 claimed sequence CN 6: PN: US20030040600 SEQID: 6 claimed protein

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MF C61 H81 N11 O18

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 477192-10-2 REGISTRY

ED Entered STN: 19 Dec 2002

CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C50 H71 N9 O17

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LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-B

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file CAPLUS		
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FULL ESTIMATED COST	36.21	128.88
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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CA SUBSCRIBER PRICE	0.00	-4.38

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FILE COVERS 1907 - 16 Sep 2005 VOL 143 ISS 13 FILE LAST UPDATED: 15 Sep 2005 (20050915/ED) New CAS Information Use Policies, enter HELP USAGETERMS for details. This file contains CAS Registry Numbers for easy and accurate substance identification. => S L7 L8 3 L7 => D BIB ABS 1-3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN 7 KX L8ΑN 2005:346796 CAPLUS DN 142:406541 ΤI Hirudin-like peptides from C-terminus of human blood clotting factor Va heavy chain as prothrombinase inhibitors for use in treatment of blood clotting disorders Kalafatis, Michael Applicat IN Cleveland State University, USA PΑ SO PCT Int. Appl., 88 pp. CODEN: PIXXD2 DTPatent LΑ English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---------------____ WO 2005034844 A2 20050421 WO 2004-US21487 PΙ 20040701 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRAI US 2003-502186P Ρ 20030912 Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDYQ, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin. L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN 7KN 2003:155110 ΑN CAPLUS 138:198622 DN TΤ Peptides derived from amino acids 307 to 356 of the human blood coaqulation factor Va as thrombin generation inhibitors Kalafatis, Michael; Mann, Kenneth Applicant IN Cleveland State University, USA PA SO U.S. Pat. Appl. Publ., 20 pp. CODEN: USXXCO DTPatent English LA FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

strictly prohibited.

ΡI	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	В2	20040309		
	US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723	•	

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

- L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN Told
- AN 2002:732142 CAPLUS
- DN 138:2631
- TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X
- AU Kalafatis, Michael; Beck, Daniel O.
- CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA
- SO Biochemistry (2002), 41(42), 12715-12728 PRALE FP CODEN: BICHAW; ISSN: 0006-2960
- PB American Chemical Society
- DT Journal
- LA English
- AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 μM . the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 μM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> file registry COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 8.40 137.28 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -2.19 -6.57

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STRUCTURE FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9 DICTIONARY FILE UPDATES: 15 SEP 2005 HIGHEST RN 863287-86-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

* The CA roles and document type information have been removed from *

* the IDE default display format and the ED field has been added, *

* effective March 20, 2005. A new display format, IDERL, is now *

* available and contains the CA role and document type information. *

*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> S (WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEEV)/SQSP AND 3-10/SQL 2 WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEEV/SQSP 583950 3-10/SQL

L9 2 (WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEEV)/SQSP AND 3-10/SQL

=> D 1-2

- L9 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 499777-67-2 REGISTRY
- ED Entered STN: 18 Mar 2003
- CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

- CN 4: PN: US20030040600 SEQID: 6 claimed sequence
- CN 6: PN: US20030040600 SEQID: 6 claimed protein
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C61 H81 N11 O18
- SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L9 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 477192-10-2 REGISTRY
- ED Entered STN: 19 Dec 2002
- CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L-a-glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

- CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C50 H71 N9 O17
- SR CA
- LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file CAPLUS COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 36.21 173.49 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL **ENTRY** SESSION CA SUBSCRIBER PRICE 0.00 -6.57

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strictly prohibited. FILE COVERS 1907 - 16 Sep 2005 VOL 143 ISS 13 FILE LAST UPDATED: 15 Sep 2005 (20050915/ED) New CAS Information Use Policies, enter HELP USAGETERMS for details. This file contains CAS Registry Numbers for easy and accurate substance identification. => S L9 L103 L9 => D BIB ABS 1-3 L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN LOW X 2005:346796 CAPLUS AN DN 142:406541 TΙ Hirudin-like peptides from C-terminus of human blood clotting factor Va heavy chain as prothrombinase inhibitors for use in treatment of blood clotting disorders twoilsof Kalafatis, Michael ΙN PA Cleveland State University, USA SO PCT Int. Appl., 88 pp. CODEN: PIXXD2 DTPatent LΑ English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE -------------------WO 2005034844 A2 WO 2004-US21487 20050421 20040701 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRAI US 2003-502186P P 20030912 Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDYQ, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin. L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN VXX AN2003:155110 CAPLUS DN 138:198622 ΤI Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va as thrombin generation inhibitors Kalafatis, Michael; Mann, Kenneth IN Eussilga PA Cleveland State University, USA SO U.S. Pat. Appl. Publ., 20 pp. CODEN: USXXCO DT Patent

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FAN.CNT 1

English

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

PΙ	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	В2	20040309		
	US 2004186271	Ą1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723		

AB Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 μM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

- L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN LONG
- AN 2002:732142 CAPLUS
- DN 138:2631
- TI Identification of a binding site for blood coagulation factor Xa on the heavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X
- AU Kalafatis, Michael; Beck, Daniel O.
- CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA
- SO Biochemistry (2002), 41(42), 12715-12728 AFTER EFD CODEN: BICHAW; ISSN: 0006-2960
- PB American Chemical Society
- DT Journal
- LA English
- AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at .apprx.230

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of 5.7 μM . the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 μM). The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> S (WEYFI|EYFIA|YFIAA|FIAAE|IAAEE|AAEEV|LDNFS)/SQSP AND 3-10/SQL 11 WEYFI|EYFIA|YFIAA|FIAAE|IAAEE|AAEEV|LDNFS/SQSP 583950 3-10/SQL



L11 11 (WEYFI|EYFIA|YFIAA|FIAAE|IAAEE|AAEEV|LDNFS)/SQSP AND 3-10/SQL

=> D 1-11

- L11 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 603110-44-7 REGISTRY
- ED Entered STN: 13 Oct 2003
- CN L-Valine, L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C21 H35 N5 O10
- SR CA
- LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L11 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 603110-42-5 REGISTRY
- ED Entered STN: 13 Oct 2003
- CN L-Alanine, $L-\alpha$ -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

- CN 23: PN: WO2005034844 SEQID: 25 unclaimed sequence
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C32 H43 N5 O9
- SR CA
- LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 2 REFERENCES IN FILE CA (1907 TO DATE)
- 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L11 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 603110-41-4 REGISTRY
- ED Entered STN: 13 Oct 2003
- CN L-Glutamic acid, L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C26 H39 N5 O8
- SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L11 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 503587-58-4 REGISTRY
- ED Entered STN: 22 Apr 2003
- CN L-Arginine, L-tyrosyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-phenylalanyl-L-seryl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 93: PN: WO03025005 FIGURE: 43 unclaimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C51 H73 N13 O19

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L11 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 499777-73-0 REGISTRY
- ED Entered STN: 18 Mar 2003
- CN L-Serine, L-leucyl-L- α -aspartyl-L-asparaginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

- CN 10: PN: US20030040600 SEQID: 12 claimed sequence
- CN 12: PN: US20030040600 SEQID: 12 claimed protein
- FS PROTEIN SEQUENCE; STEREOSEARCH
- MF C26 H38 N6 O10
- SR CA
- LC STN Files: CA, CAPLUS, USPAT7, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L11 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 499777-72-9 REGISTRY
- ED Entered STN: 18 Mar 2003
- CN L-Serine, L-tyrosyl-L-arginyl-L-seryl-L-glutaminyl-L-histidyl-L-leucyl-Lα-aspartyl-L-asparaginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 11: PN: US20030040600 SEQID: 11 claimed protein

CN 9: PN: US20030040600 SEQID: 11 claimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C55 H79 N17 O18

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

- L11 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 499777-68-3 REGISTRY
- ED Entered STN: 18 Mar 2003
- CN L-Alanine, L-alanyl-L-a-glutamyl-L- α -glutamyl-L-valyl-L-isoleucyl-L-tryptophyl-L- α -aspartyl-L-tyrosyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 5: PN: US20030040600 SEQID: 7 claimed sequence CN 7: PN: US20030040600 SEQID: 7 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C54 H75 N11 O18

SR CA

LC STN Files: CA, CAPLUS, USPATZ, USPATFULL

Absolute stereochemistry.

PAGE 1-A

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 499777-67-2 REGISTRY

ED Entered STN: 18 Mar 2003

CN L-Valine, L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4: PN: US20030040600 SEQID: 6 claimed sequence

CN 6: PN: US20030040600 SEQID: 6 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C61 H81 N11 O18

SR CA

LC STN Files: CA, CAPLUS, USPAT7, USPATFULL

Absolute stereochemistry.

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 499777-66-1 REGISTRY

ED Entered STN: 18 Mar 2003

CN L-Isoleucine, L-arginyl-L-histidyl-L-methionyl-L-lysyl-L-arginyl-L-tryptophyl-L- α -glutamyl-L-tyrosyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3: PN: US20030040600 SEQID: 5 claimed sequence

CN 5: PN: US20030040600 SEQID: 5 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C69 H100 N20 O14 S

SR CA

LC STN Files: CA, CAPLUS, USPATZ, USPATFULL

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 477192-10-2 REGISTRY

ED Entered STN: 19 Dec 2002

CN L-Valine, L- α -glutamyl-L-tyrosyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl- (9CI) (CA INDEX NAME) OTHER NAMES:

CN 22: PN: WO2005034844 SEQID: 24 unclaimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C50 H71 N9 O17

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry. .

PAGE 1-A

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 321875-41-6 REGISTRY

ED Entered STN: 15 Feb 2001

CN L-Tryptophan, L-isoleucyl-L-alanyl-L-alanyl-L- α -glutamyl-L- α -glutamyl-L-asparaginyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1126: PN: WOO104316 PAGE: 63 claimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C37 H53 N9 O13

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

= 326-330 of Feebox Vo.

ORF 41a ?

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file CAPLUS COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

52.77 234.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL ENTRY SESSION

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=> S L11

L12 6 L11

=> D BIB ABS <u>1-6</u>

5×4

L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:346796 CAPLUS

DN 142:406541

TI Hirudin-like peptides from C-terminus of human blood clotting factor Va heavy chain as prothrombinase inhibitors for use in treatment of blood clotting disorders

IN Kalafatis, Michael

Applicant

PA Cleveland State University, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE

DATE APPLICATION NO. DATE _____ 20050421 PI WO 2005034844 A2 WO 2004-US21487 20040701 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-502186P P 20030912

AB Disclosed are peptides from the carboxy terminus of the human blood clotting factor Va which significantly inhibit thrombin generation. Also disclosed are pharmaceutical compns. containing these peptides and related therapeutic methods for inhibiting thrombin generation and treating blood coagulation disorders. Thus, peptides DYDY and DYDYQ, and sulfonated derivs. thereof, compete with prothrombinase for binding to prothrombin.

- L12 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN 500
- AN 2003:556837 CAPLUS
- DN 139:257136
- TI Amino Acids Glu323, Tyr324, Glu330, and Val331 of Factor Va Heavy Chain Are Essential for Expression of Cofactor Activity
- AU Singh, Lisam S.; Bukys, Michael A.; Beck, Daniel O.; Kalafatis, Michael
- CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA
- Journal of Biological Chemistry (2003), 278(30), 28335-28345 After EFD CODEN: JBCHA3; ISSN: 0021-9258
- PB American Society for Biochemistry and Molecular Biology
- DT Journal
- LA English
- AΒ We have recently demonstrated that amino acid region 323-331 of factor Va heavy chain (9 amino acids, AP4') contains a binding site for factor Xa (Kalafatis, M., and Beck, D. O. (2002) Biochem. 41, 12715-12728). ascertain which amino acids within this region are important for the effector and receptor properties of the cofactor with respect to factor Xa, we have synthesized three overlapping peptides (5 amino acids each) spanning the amino acid region 323-331 and tested them for their effect on prothrombinase complex assembly and function. Peptide containing amino acids 323EYFIA327 alone was found to increase the catalytic efficiency of factor Xa but had no effect on the fluorescent anisotropy of active site-labeled factor Xa (human factor Xa labeled in the active site with Oregon Green 488; [OG488]-EGR-hXa). In contrast, peptide containing the sequence 327AAEEV331 was found to interact with [OG488]-EGR-hXa with half-maximal saturation reached at .apprx.150 µM, but it was unable to produce a cofactor effect on factor Xa. Peptide 325FIAAE329 inhibited prothrombinase activity and was able to partially decrease the fluorescent anisotropy of [OG488]-EGR-hXa but could not increase the catalytic efficiency of factor Xa with respect to prothrombin. A control peptide with the sequence FFFIA did not increase the catalytic efficiency of factor Xa, whereas a peptide with the sequence Emi was impaired in its capability to interact with [OG488]-EGR-hXa. Two mutant recombinant factor Va mols. (Glu323 Phe/Tyr324 Phe, factor VaFF; Glu330 Met/Val331 Ile, factor VaMI) showed impaired cofactor activity when used at limiting cofactor concentration,

the quadruple mutant (Glu323 Phe/Tyr324 Phe and Glu330 Met/Val331Ile, factor VaFF/MI) had no cofactor activity under similar exptl. conditions. Our data demonstrate that amino acid residues Glu323, Tyr324, Glu330, and Val331 of factor Va heavy chain are critical for expression of factor Va cofactor activity.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN SCO
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AN 2003:242369 CAPLUS

DN 138:283309

- TI Cloning, purification and characterization of enzymes from pathogenic bacteria involved in protein processing and drug screening and drug design applications
- IN Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala, Megan; Kanagarajah, Dhushy; Li, Qin; Mansoury, Kamran; Necakov, Sasha; Nethery, Kathleen; Ng, Ivy; Pinder, Benjamin; Sheldrick, Bay; Vallee, Francois; Viola, Cristina; Wrezel, Olga; et al.
- PA Affinium Pharmaceuticals, Inc., Can.
- SO PCT Int. Appl., 273 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

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APPLICATION NO.
                                DATE
    PATENT NO.
                        KIND
                                                                    DATE
                                -----
    WO 2003025005 A2 20030327
WO 2003025005 A3 20040311
                                          WO 2002-CA1426
                                                                    20020920
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                             20010921
PRAI US 2001-324135P
    US 2001-324139P
                                20010921
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                                            After EFD
    US 2001-325333P
                                20010927
                         Ρ
    US 2001-325836P
                         Ρ
                                20010928
    US 2001-338235P
                         Р
                                20011025
                         P 20011025
    US 2001-343758P
    US 2001-340531P
                         ₽
                                20011026
    US 2001-340945P P
US 2001-333281P P
US 2002-399926P P
                                20011030
                                20011106
                                20020731
    US 2002-399926P
                        P
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AB The present invention relates to polypeptide targets for pathogenic bacteria. A number of antimicrobial target enzymes have been identified, expressed, and purified from Staphylococcus aureus, Helicobacter pylori, Streptococcus pneumoniae, and Escherichia coli. Cloning, the nucleotide sequences and the encoded amino acid sequences of genes clpL, cysM, pepP, kdsA, secA, trmD, ilvE, aroB, and glyA from S. aureus, H. pylori, S. pneumoniae, and E. coli are disclosed. The invention also provides biochem. and biophys. characteristics of those polypeptides. The polypeptides are characterized by using mass spectrometry, NMR, x-ray crystallog., and bioinformatics anal. The polypeptides of the invention can be used for drug screening, drug design, in diagnostic assays and in pharmacol. applications.

L12 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:155110 CAPLUS

- DN 138:198622
- Peptides derived from amino acids 307 to 356 of the human blood ΤI coagulation factor Va as thrombin generation inhibitors Kalafatis, Michael; Mann, Kenneth Applicant
- IN
- PA Cleveland State University, USA
- SO U.S. Pat. Appl. Publ., 20 pp. CODEN: USXXCO
- DTPatent
- LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	US 2003040600	A1	20030227	US 2001-911129	20010723
	US 6703364	B2	20040309		
	US 2004186271	A1	20040923	US 2004-795795	20040308
PRAI	US 2001-911129	A3	20010723		

AΒ Peptides derived from amino acids 307 to 356 of the human blood coagulation factor Va are provided. Such peptides comprise: (i) a length of between 3 and 50 amino acids, (ii) a min. of 3 contiguous amino acids from the 307-356 heavy chain region of factor Va, excluding peptide segments comprising amino acids 311 to 325 and amino acids 321 to 335, (iii) optional addnl. amino acids at one or both ends of the contiguous amino acids such that the entire peptide is at least 60% identical to a sequence within 307 to 356 of factor Va, and (iv) have an IC50 of between 50 nM to 500 µM for inhibition of prothrombinase. The present invention also provides a pharmaceutical composition comprising one or more prothrombinase-inhibiting peptide segments. The present invention also provides administration of the pharmaceutical composition to human subjects for the purpose of preventing thrombotic disorders.

- L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
- 2002:732142 CAPLUS ΑN
- DN 138:2631
- Identification of a binding site for blood coagulation factor Xa on the TIheavy chain of factor Va. Amino acid residues 323-331 of factor V represent an interactive site for activated factor X
- ΑU Kalafatis, Michael; Beck, Daniel O.
- CS Department of Chemistry, Cleveland State University, Cleveland, OH, 44115, USA
- Biochemistry (2002), 41(42), 12715-12728 Atta EFD SO CODEN: BICHAW; ISSN: 0006-2960
- PB American Chemical Society
- DTJournal
- LΑ English
- AB The authors have recently shown that amino acid region 307-348 of factor Va heavy chain (42 amino acids, N42R) is critical for cofactor activity and may contain a binding site for factor Xa and/or prothrombin. To ascertain the importance of this region for factor Va cofactor activity, the authors have synthesized eight overlapping peptides (10 amino acid each) spanning amino acid region 307-351 of the heavy chain of factor Va and tested them for inhibition of prothrombinase activity. The peptides were also tested for the inhibition of the binding of factor Va to membrane-bound active site fluorescent labeled Glu-Gly-Arg human factor Xa ([OG488]-EGR-hXa). Factor Va binds specifically to membrane-bound [OG488]-EGR-hXa (10 nM) with half-maximum saturation reached at .apprx.6 nM. N42R was also found to interact with [OG488]-EGR-hXa with half-maximal saturation observed at

nM peptide. N42R was found to inhibit prothrombinase activity with an IC50 of .apprx.250 nM. A nonapeptide containing amino acid region 323-331 of factor Va (AP4') was found to be a potent inhibitor of prothrombinase. Kinetic analyses revealed that AP4' is a noncompetitive inhibitor of prothrombinase with respect to prothrombin, with a Ki of $5.7 \mu M$. the peptide interferes with the factor Va-factor Xa interaction. Displacement expts. revealed that the nonapeptide inhibits the direct

interaction of factor Va with [OG488]-EGR-hXa (IC50 .apprx.7.5 $\mu M)$. The nonapeptide was also found to bind directly to [OG488]-EGR-hXa and to increase the catalytic efficiency of factor Xa toward prothrombin in the absence of factor Va. In contrast, a peptadecapeptide from N42R encompassing amino acid region 337-351 of factor Va (P15H) had no effect on either prothrombinase activity or the ability of the cofactor to interact with [OG488]-EGR-hXa. The authors' data demonstrate that amino acid sequence 323-331 of factor Va heavy chain contains a binding site for factor Xa.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L12 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN 5XX
      2001:50820 CAPLUS
 DN
      134:126821
 ΤI
      Antigenic determinants of antigenic proteins of Neisseria meningitidis and
      their diagnostic, prophylactic and therapeutic use
      Masignani, Vega; Scarlato, Vincenzo; Scarselli, Maria; Galeotti, Cesira;
 ΤN
      Mora, Mariarosa
      Chiron S.p.A., Italy
 PA
      PCT Int. Appl., 80 pp.
 SO
      CODEN: PIXXD2
 DT
      Patent
 LΑ
      English
 FAN.CNT 1
      PATENT NO.
                         KIND
                                 DATE
                                            APPLICATION NO.
                                                                    DATE
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      WO 2001004316 A2 20010118 WO 2001004316 A3 20010809.
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                                            WO 2000-IB1026
                                                                    20000713
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              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
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              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
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      CA 2378547
                              20010118 CA 2000-2378547
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                                                                    20000713
                                          EP 2000-944161
      EP 1196587
                                 20020417
                          A2
                                                                    20000713
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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      BR 2000012424
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      RU 2253678
                                 20050610
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                                 19990714
20000713 7GB9914529.2 102B *
🗙 PRAÎ
      GB 1999-16529
      WO 2000-IB1026
 AB
      Antigenic determinants of known antigenic proteins of Neisseria
      meningitidis are characterized. The peptides can be used as diagnostic
```

AB Antigenic determinants of known antigenic proteins of Neisseria meningitidis are characterized. The peptides can be used as diagnostic reagents or as antigens for vaccines and they may be manufactured by expression of a natural or synthetic gene encoding the protein. Homologous sequences and proteins comprising these fragments are also disclosed.

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COST IN U.S. DOLLARS
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                                                                TOTAL
                                                     ENTRY
                                                              SESSION
FULL ESTIMATED COST
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CA SUBSCRIBER PRICE
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=> S (WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS)/SQSP AND 3-10/SQL 170 WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS/SQSP 583950 3-10/SQL

400

L13 170 (WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS)/SQSP AND 3-10/SQL

=> file CAPLUS		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	32.53	283.54
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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FULL ESTIMATED COST 0.45 283.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION
CA SUBSCRIBER PRICE

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-13.14

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

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39X

583950 3-10/SQL L15 4544 (WEY|EYF|YFI|FIA|IAA|AAE|AEE|EEV|LDN|DNF|NFS)/SQSP AND 3-10/SQL

=> file CAPLUS COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 32.53 316.52

SINCE FILE ENTRY TOTAL

CA SUBSCRIBER PRICE

ENTRY SESSION -13.14

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=> dis his

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L10

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L2 34303 S S1

L3 3 S L1

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L5 3 S L1

L6 3 S L4

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L7 2 S (WEYFIAA|EYFIAAE|YFIAAEE|FIAAEEV)/SQSP AND 3-10/SQL

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L8 3 S L7

FILE 'REGISTRY' ENTERED AT 13:48:53 ON 16 SEP 2005

L9 2 S (WEYFIA|EYFIAA|YFIAAE|FIAAEE|IAAEEV)/SQSP AND 3-10/SQL

FILE 'CAPLUS' ENTERED AT 13:49:41 ON 16 SEP 2005 3 S L9

FILE 'REGISTRY' ENTERED AT 13:50:08 ON 16 SEP 2005
L11 11 S (WEYFI|EYFIA|YFIAA|FIAAE|IAAEE|AAEEV|LDNFS)/SQSP AND 3-10/SQL

FILE 'CAPLUS' ENTERED AT 13:50:44 ON 16 SEP 2005

L12 6 S L11

FILE 'REGISTRY' ENTERED AT 13:51:08 ON 16 SEP 2005

L13 170 S (WEYF|EYFI|YFIA|FIAA|IAAE|AAEE|AEEV|LDNF|DNFS)/SQSP AND 3-10/

FILE 'CAPLUS' ENTERED AT 13:51:45 ON 16 SEP 2005

L14 121 S L13

FILE 'REGISTRY' ENTERED AT 13:52:03 ON 16 SEP 2005

L15 4544 S (WEY|EYF|YFI|FIA|IAA|AAE|AEE|EEV|LDN|DNF|NFS)/SQSP AND 3-10/S

FILE 'CAPLUS' ENTERED AT 13:52:40 ON 16 SEP 2005

L16 1915 S L15

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD: y

COST IN U.S. DOLLARS SINCE FILE TOTAL

ENTRY SESSION

FULL ESTIMATED COST 0.45 316.97

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

ENTRY SESSION

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STN INTERNATIONAL LOGOFF AT 13:53:28 ON 16 SEP 2005

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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6 AUG 30 NEWS CA/CAplus - Increased access to 19th century research documents

NEWS 7 AUG 30 CASREACT - Enhanced with displayable reaction conditions

NEWS SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY

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=> s deltrophin##

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=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci COST IN U.S. DOLLARS SINCE FILE TOTAL

ENTRY SESSION 0.21

0.21

FULL ESTIMATED COST

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